

I. Amendments

By this amendment, claims 1, 2, 4, 6, 16, 22, 25-29 and 31-39 have been amended, new claims 40 and 41 have been added and claims 3, 17-21 and 30 have been canceled.

This amendment adds no new matter to the specification. Support for this amendment is found in the specification and claims as filed.

Specifically, support for the modification to page 9, paragraph 4 may be found in the title compound of Example 25; support for the modification to page 14, paragraph 1 may be found at page 5, line 14 and in the title compound of Example 94; and support for the modification to page 17, paragraph 3 may be found at page 5, lines 1 and 2 and in the titled compounds of Examples 45 and 49.

Support for new claims 40 and 41 may be found at page 37, lines 15-24 *inter alia*.

Typographical errors have also been corrected in the specification.

No change of inventorship is necessitated by this amendment.

II. Discussion of the Restriction Requirement

A restriction requirement has been imposed on the pending claims.

By this amendment, R¹ and R² have been limited to formation of certain six-membered nitrogen-containing rings. Specifically, R¹ and R² have been limited to forming in combination, together with an adjacent nitrogen atom, a 1-piperidinyl, 1-homopiperidinyl, 1-piperazinyl or 1-homopiperazinyl ring optionally having a substituent or substituents in independent claims 1, 26 and 27. In conjunction with these changes, dependent claims 2, 4, 6, 31 and 33 have also been modified and claims 3 and 30 have been cancelled. This amendment adds no new matter to the specification. Support for the amendment may be found at page 9, lines 14-16 *inter alia*.

In addition, Applicants contend that claims 25 and 29 should not have been withdrawn. Rather, Applicant should have been given the opportunity to re-write the

claims. Accordingly, Applicants have re-written claims 25 and 29 as method claims, and respectfully request reconsideration of the withdrawal of these claims.

III. Discussion of the 35 U.S.C. Sec. 112, Second Paragraph Rejection of Claim 1

Claim 1 has been rejected under 35 U.S.C. Sec. 112, second paragraph as allegedly indefinite in the use of the phrase “hydrocarbon optionally having a substituent or substituents”. Applicants respectfully traverse this rejection.

As an initial matter, Applicants note that this phrase appears in the description of variables for R^3 , R^4 , E, Q and R; and that the phrase appears in independent claims 1, 26 and 27.

Applicants assert that the phrase is sufficiently clear and would be understood by those skilled in the art in light of the teachings of the specification. In particular, hydrocarbon groups are defined on page 7, lines 19-23. Optional substituents of the hydrocarbon group are defined on page 13, lines 6-34.

One skilled in the art would understand that the term “hydrocarbon” applies to the base substituent, wherein when that substituent has substituents, they may include groups outside of hydrocarbons. That is to say that the Examiner’s uncertainty about whether or not non-hydrocarbon substituents of the hydrocarbon substituent are within the scope of the claim is unfounded. Those skilled in the art would understand that a hydrocarbon substituent could itself have non-hydrocarbon substituents, given the teachings of the specification.

Therefore Applicants respectfully request withdrawal of the 35 U.S.C. Sec. 112, second paragraph rejection of claim 1.

IV. Discussion of the 35 U.S.C. Sec. 112, Second Paragraph Rejection of Claims 16-24

Claims 16-24 have been rejected under 35 U.S.C. Sec. 112, second paragraph as allegedly indefinite. Applicants respectfully traverse this rejection.

By this amendment, claim 16 has been modified to remove the term “pharmaceutical”. Applicants assert that the broader composition claim is not required to include quantitative limitations.

Claims 17-21 have been cancelled.

As to the remaining claims 22-24, claim 22 (now dependent upon claim 16) recites protease inhibitors and/or reverse transcriptase inhibitors as components of the composition which are additional to the components recited in claim 16. Claims 23 and 24 (dependent upon claim 22) further specify specific reverse transcriptase inhibitors and protease inhibitors respectively. The compositions, as well as compositions in combination with additional components are described on page 35, line 24- page 37, line 14. Dosages for the additional components recited in claims 23 and 24 are specified on page 37, line 33- page 38, line 20. Specific embodiments are provided on page 38, lines 21- 33.

Therefore, Applicants respectfully request withdrawal of the 35 U.S.C. Sec. 112, second paragraph rejection of claims 16-24.

V. Discussion of the 35 U.S.C. Sec. 112, First Paragraph Rejection of Claim 15

Claim 15 has been rejected under 35 U.S.C. Sec. 112, first paragraph as allegedly not enabled as to the term “pro-drug”. Applicants respectfully traverse the rejection.

As an initial matter, Applicants note that claims 16 and 25 also contain this term.

Applicants have defined pro-drugs in the specification at page 26, lines 12-33. Therefore the term “pro-drug” is adequately enabled by the specification and respectfully request withdrawal of the 35 U.S.C. Sec. 112, first paragraph rejection of claim 15.

VI. Discussion of the 35 U.S.C. Sec. 112, First Paragraph Rejection of Claim 28

Claim 28 has been rejected under 35 U.S.C. Sec. 112, first paragraph as allegedly not enabled.

By this amendment, claim 28 has been modified to recite “CCR5 receptor activity”. This amendment adds no new matter to the specification. Support for the amendment may be found at page 106, line 33 – page 108, line 24 *inter alia*.

Therefore Applicants respectfully request withdrawal of the 35 U.S.C. Sec. 112, first paragraph rejection of claim 28.

VII. Discussion of the 35 U.S.C. Sec. 112, First Paragraph Rejection of Claims 22-24

Claims 22-24 have been rejected under 35 U.S.C. Sec. 112, first paragraph as allegedly lacking enablement. Applicants respectfully traverse the rejection.

As indicated above, claim 22 (now dependent upon claim 16) recites protease inhibitors and/or reverse transcriptase inhibitors as components of the composition which are additional to the components recited in claim 16. Claims 23 and 24 (dependent upon claim 22) further specify specific reverse transcriptase inhibitors and protease inhibitors respectively. The compositions, as well as compositions in combination with additional components are described on page 35, line 24- page 37, line 14. Dosages for the additional components recited in claims 23

and 24 are specified on page 37, line 33- page 38, line 20. Specific embodiments are provided on page 38, lines 21- 33.

Therefore, Applicants respectfully request withdrawal of the 35 U.S.C. Sec. 112, first paragraph rejection of claims 22-24.

VIII. Discussion of Claims 31-39

By this amendment, claims 31-39 have been modified to depend upon method claim 28. Therefore, they are not essential duplicates of claims 4-12. Applicants assert that due to this modification, cancellation of one of the sets of claims is unnecessary.

IX. Discussion of the 35 U.S.C. Sec. 103(a) Rejection over Kato *et al.*

Claims 1-13, 15, 16 and 30-39 have been rejected under 35 U.S.C. Sec. 103(a) as allegedly obvious over Kato *et al.*, WO 01/21577. Applicants respectfully traverse the rejection.

A Certified Copy of an English-language translation of the priority Japanese patent application accompanies this response. Applicants respectfully request reconsideration of the appropriateness of the cited reference as proper art in light of their perfected priority.

X. Discussion of the 35 U.S.C. Sec. 103(a) Rejection over Weber *et al.* in view of Chepkova *et al.* and Patani *et al.*

Claims 1-16 and 30-39 have been rejected under 35 U.S.C. Sec. 103(a) as allegedly obvious over Weber *et al.*, U.S. Patent No. 4,891,378 in view of Chepkova *et al.*, Chem Abs. 1991:157055 and Patani *et al.* in Chem. Rev. 1996, 96, 3147-3176. Applicants respectfully traverse the rejection.

The '378 reference is directed to substituted pyrrolidinones. The compounds recited in independent claim 1 as amended differ from the compounds of the cited reference. One point of differentiation is the chain $-G-NR^3-E-NR^1R^2$ of the presently claimed compounds. For the present invention, E is a divalent chain hydrocarbon group and G is CO or SO₂. In the cited reference, the chain of $-CH_2-NR_2-CO-NR_3R_4$ is found in Formula I. As the Examiner has understood, these two chains are dissimilar. Therefore, the Applicants' invention, as set forth in the claims as amended, is neither taught nor suggested by Weber *et al.*

The deficiencies of Weber *et al.* are not cured by Patani *et al.* The Patani *et al.* article discloses functional groups which are listed as possible bioisosteric replacements for an amide bond. From this teaching, the Examiner has concluded that the present compounds would be obvious through linker modification (as indicated in Patani *et al.*) of the Weber *et al.* chain.

This assumption is faulty. Applicants note that (1) if the "reversed amide" in the Patani *et al.* reference, Table 48, replaces the amide in the compounds of the Weber *et al.* reference, the chain of $-CH_2-CO-NR_2-NR_3R_4$ would be theoretically created or (2) if the "amide homologue" in the Patani *et al.* reference, Table 48, replaces the amide in the compounds of the Weber *et al.* reference, the chain of $-CH_2-CH_2NR_2CO-NR_3R_4$ would be theoretically created. Neither substitution teaches or suggests any portion of Applicants' invention. If the Examiner is thinking of some other specific substitution, the Examiner is kindly requested to inform Applicants of the same.

Therefore, the combined teaching of the Weber *et al.* and Patani *et al.* references do not render the Applicants' invention, as set forth in the present claims as amended, obvious.

The deficiencies of Weber *et al.* and Patani *et al.* are not cured by Chepkova *et al.* Chepkova *et al.* discloses a compound having a linking unit of $-CO-NH-CH(Me)-$. However,

neither the right-hand side nor the left-hand side of the compound of the cited reference is the same as that of the compounds presently claimed in independent claim 1.

Therefore, the compounds set forth in independent claim 1 as amended are not taught or suggested by the combined teachings of the cited reference.

Moreover, Applicants submit that the five specific compounds and salts thereof recited in independent claim 14 are neither taught nor suggested by the combined teachings of the cited references.

Claims 2, 4-13, 15, 16 and 31-39 depend upon claim 1. Applicants submit that the more specific dependent claims are also non-obvious for the reasons provided above.

Claims 3 and 30 have been cancelled.

Therefore Applicants respectfully request withdrawal of the 35 U.S.C. Sec. 103(a) rejection over Weber *et al.* in view of Chepkova *et al.* and Patani *et al.*

XI. Discussion of the 35 U.S.C. Sec. 103(a) Rejection over Kim *et al.* in view of Caldwell *et al.*

Claims 1-13, 15-24, 26-28 and 30-39 have been rejected under 35 U.S.C. Sec. 103(a) as allegedly obvious over Kim *et al.*, U.S. Patent No. 6,511,994 in view of Caldwell *et al.*, U.S. Patent No. 6,136,827. Applicants respectfully traverse the rejection.

A Certified Copy of an English-language translation of the priority Japanese patent application accompanies this response. Applicants respectfully request reconsideration of the appropriateness of the Kim *et al.* reference as proper art in light of their perfected priority.

XII. Conclusion

Reconsideration of the claims as amended and allowance is requested.

Should the Examiner believe that a conference with Applicants' attorney would advance prosecution of this application, she is respectfully invited to call Applicants' attorney at the number below.

Respectfully submitted,

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